Docket No. 20488/44-DIV-CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:

Demuth et al.

ART UNIT:

Not yet assigned

SERIAL NO.:

10/676,832

FILED:

October 1, 2003

FOR: METHOD FOR THE IMPROVEMENT OF ISLET

SIGNALING IN DIABETES MELLITUS AND FOR ITS

PREVENTION

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Sandra J. Wittrup

November 19,2003

INFORMATION DISCLOSURE STATEMENT SUBMITTING REFERENCES ON COMPACT DISC

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Date: November 19, 2003

Pursuant to Applicant(s) duty of disclosure, the information listed in the attached form PTO-1449 is brought to the attention of the Examiner.

The citation of the listed items is not a representation that they constitute a complete or exhaustive listing of the relevant art or that the references are prior art. The items listed are submitted in good faith, but are not intended to substitute for the Examiner's search. It is hoped, however, that in addition to apprising the Examiner of these particular items, they will assist in identifying fields of search and in making as full and complete a search as possible.

The filing of this information disclosure statement is not an admission that the information cited herein is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

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In accordance with the requirement under 37 C.F.R. 1.98 (3)(i), the following are concise explanations of the relevance, as presently understood, with regard to those items submitted herewith that are not in the English language:

I. LIST OF PATENTS, PUBLICATIONS OR OTHER INFORMATION

The patents, publications or other information submitted for consideration by the Office are listed on PTO-1449, attached hereto.

II. COPIES

a. Submitted herewith on Compact Disc is a legible copy of (i) each U.S and foreign patent; (ii) each publication or that portion which caused it to be listed; and (iii) all other information or that portion which caused it to be listed.

III. CONCISE EXPLANATION OF THE RELEVANCE

(check at least one box)

- a. Except as may be indicated below in (b), all of the patents, publications or other information are in the English language or were cited in an English language Search Report, a copy of which is attached hereto (concise explanation not required).
- b. A concise explanation of the relevance of all patents, publications or other information listed that is not in the English language is as follows:

FRENCH LANGUAGE FR 2 696 740 Applicants have relied on an English language abstract in determining that this patent apparently relates to Dimethylbiguanide drug derivatives and their medical applications.

FRENCH LANGUAGE FR 2 085 665 Applicants have relied on an English language abstract in determining that this patent apparently relates to biguanide substitutes possessing a hypoglycemic property.

GERMAN LANGUAGE DT 25 42 598 A1 Applicants have relied on an English language abstract in determining that this patent apparently relates to biguanide salts as well as a method for preparing such salts. In addition to this the invention apparently covers pharmaceutical compounds which contain such salts.

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GERMAN LANGUAGE WO 97/40832 Applicants have relied on an English language abstract in determining that this patent apparently relates to the use of a method for reducing in the blood of a mammal by administration of effectors the enzyme activity of dipeptidyl peptidase (DP IV) or enzyme activity similar to DP IV, the endogenous (or additionally exogenously administered) insulinotropic peptide gastric inhibitory polypeptide 1-42 and glucagon-like peptide amide-1 7-36 are decomposed in a causal sequence to a reduced extent by DP IV enzymes or those similar to DP IV.

JAPANESE PATENT JP 4-334357A2: Applicants have relied on an English language abstract in determining that this patent ACYL DERIVATIVE HAVING ENZYME-INHIBITING ACTION, apparently relates to a compound having a prolyl endopeptibase activity-inhibiting action and useful as an antidement agent, especially an anti-amnestic agent.

GERMAN LANGUAGE DE 299 09 210 U1 Applicants have relied on an English language abstract in determining that this patent apparently relates to dipeptide compounds or compounds analogous to dipeptide compounds, which are made of an amino acid and a thiazolidine or pyrrolidine group, and to their salts. The invention further relates to the use of these compounds in the treatment of impaired glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, diabetic neuropathy and nephropathy as well as secondary diseases of diabetes mellitus in mammals.

GERMAN LANGUAGE DE 198 26 972 A1 Applicants have relied on an English language abstract in determining that this patent apparently relates to the use of inhibitors (I) of dipeptidyl peptidase IV (DP IV) or analogous enzymes for inhibiting the activation and proliferation of keratinocytes (including malignantly transformed keratinocytes) and tumor cells derived from keratinocytes.

GERMAN LANGUAGE WO 99/61431 Applicants have relied on an English language abstract in determining that this patent apparently relates to dipeptide compounds or compounds analogous to dipeptide compounds, which are made of an amino acid and a thiazolidine or pyrrolidine group, and to their salts. The invention further relates to the use of these compounds in the treatment of impaired glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, diabetic neuropathy and nephropathy as well as secondary diseases of diabetes mellitus in mammals.

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	с. 🗌	The following additional information is provided for the Examiner's consideration:
		<u>FEES</u>
IV.		OS IS BEING FILED UNDER 37 C.F.R. § 1.97(b) one box)
	a. 🔀	within three months of the filing date of a national application (37 C.F.R. § 1.97(b) (1)). No fee or certification is required.
	b	within three months of the date of entry of the national stage as set forth in §1.491 in an international application (37 C.F.R. § 1.97(b) (2)). No fee or certification is required.
	c. 🗌	before the mailing date of a first Action on the merits (37 C.F.R. § 1.97(b) (3)). No fee or certification is required. In the event that a first Office Action on the merits has been issued, please consider this IDS under 37 C.F.R. § 1.97(c) and see the certification under 37 C.F.R. § 1.97(e) below, or, if no certification has been made, charge our deposit account a fee in the amount of \$180.00 as required by 37 C.F.R. § 1.17(p).
V.		OS IS BEING FILED UNDER 37 C.F.R. § 1.97(c): one box)
	1.97(c)	he mailing date of a Final Office Action under 37 C.F.R. § 1.113 (See 37 C.F.R. § (1)) or before the mailing date of a Notice of Allowance under 37 C.F.R. § 1.311 C.F.R. § 1.97(c) (2)).
	a. 🔲 🗆	No certification; therefore, a fee in the amount of \$180.00 is required by 37 C.F.R. § 1.17(p).
	b	or See the certification below. No fee is required.
VI.	CERTI	FICATION UNDER 37 C.F.R. § 1.97(e) (check only one box)
The u	ndersigne	ed hereby certifies that
	a. 🗌	each item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS; or
	b. 🗌	no item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application or, to the best of my knowledge after making reasonable inquiry, was known to any

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		to the filing of this statement.
	c. 🗌	Some of the items of information were cited in a communication from a foreign Patent Office as indicated in the Form 1449 by those references having an asterisk(*). As to this information, the undersigned certifies that each item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS. As to the remaining information, the undersigned hereby certifies that no item of this remaining information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application or, to the best of my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this statement.
		eck in the amount of \$180.00 is enclosed for the above-indicated fee. A
\boxtimes		cate copy of this paper is attached. ee is required.
VII.	THIS IDS IS	BEING FILED UNDER 37 C.F.R. § 1.704(d) (PATENT TERM
	Applies to or	riginal applications (other than design) filed on or after May 29, 2000.
a.		Each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a
		counterpart application and this communication was not received by any
		individual designated in § 1.56(c) more than thirty days prior to the filing
		of the Information Disclosure Statement.
b.	_X_	Enclosed herewith is form PTO-1449.
c.	_X	Copies of cited references are enclosed on a Compact Disc.
d.		The listed references were cited in the enclosed International Search
		Report in a counterpart foreign application.

If the Examiner has any questions concerning this IDS, the Examiner is requested to contact the undersigned. If it is determined that this IDS has been filed under the wrong rule, the

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PTO is requested to consider this IDS under the proper rule (with a petition, if necessary) and charge any additional fees to Deposit Account No. 50-0369.

Date: November 19, 2003

Respectfully submitted,

John C. Serio, Reg. No. 39,023

BROWN RUDNICK BERLACK ISRAELS LLP

Attorney(s) for Applicants

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT			ATTY. DOCKET NO. 20488/44-DIV-CON		ERIAL NO. 10/676,832	•		
				APPLICANT(S): Demuth et al.				
				FILING DATE: October 1, 2003	ART UNIT: Not Yet Assigned		ed	
			UNITED STAT	ES PATENT DOCUMENTS				
EXAM. INITIAL		DOCUMENT NUMBER	DATE	INVENTOR	CLASS	SUB CLASS	FIL. DATE IF . APPR	
WW	AA	2,961,377	11/22/1960	Shapiro et al.	167	65		
1	AB	3,174,901	03/23/1965	Sterne	167	65		
	AC	3,879,541	04/22/1975	Kabbe et al.	424	326		
	AD	3,960,949	06/01/1976	Ahrens et al.	260	564 B		
	AE	4,028,402	06/07/1977	Fischer et al.	260	501.14		
	AF	4,935,493	06/19/1990	. Bachovchin et al.	530	331	ļ	
	AG	5,433,955	07/18/1995	Bredehorst et al.	424	94.3		
	AH	5,462,928	10/31/1995	Bachovchin et al.	514	19		
	AI	5,512,549	04/30/1996	Chen et al.	514	12		
	AJ	5,543,396	08/06/1996	Powers et al.	514	. 19		
	AK	5,614,379	03/25/1997	MacKellar	435	68.1		
	AL	5,624,894	04/29/1997	Bodor	514	2		
	AM	5,939,560	08/17/1999	Jenkins et al.	548	535		
	AN	6,006,753	12/28/1999	Efendic	128	898		
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	AP	6,201,132 B1	03/13/2001	Jenkins et al.	548	535	04/21/99	
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	AR	6,500,804 B2	12/31/2002	Demuth et al.	514	19	12/31/02	
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	AT	6,011,155	01/04/2000	Villhauer	544	333		
	AU	6,107,317	08/22/2000	Villhauer	514	365		
	AV	6,110,949	08/29/2000	Villhauer	514	365		
	ΑŴ	6,124,305	09/26/2000	Villhauer	514	272		
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IN	FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT			ATTY. DOCKET NO. 20488/44-DIV-CON		ERIAL NO. 10/676,832	
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-				FILING DATE: October 1, 2003		ART UNIT: Yet Assign	ed
		•	UNITED STAT	ES PATENT DOCUMENTS			
TW	AY	5,705,483	01/06/1998	Galloway et al.	514	12	
	AZ	2001/0025023 A1	09/27/2001	Сагт	514	2	
16	AAA	6,548,481 B1	04/15/2003	Demuth et al.	514	19	11/28/00
	*		FOREIGN I	PATENT DOCUMENTS			
160		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRAN Y/N
1	. BA	WO 01/62266 A2	08/30/2001	PCT	A61K	38/00	Y
	ВВ	WO 00/53171	09/14/2000	PCT	A61K	31/155	• Ү
	ВС	DT 25 42 598 A1	04/22/1976	Germany	C07C	129/16	N
	BD	FR 2 696 740 A1	04/15/1994	France	C07D	207/404	N
	BE	FR 2 085 665	12/31/1971	France	A61K	27/00	N
	BF	WO 97/40832	11/06/1997	РСТ	A61K	31/425	Abstract only
	BG	WO 95/15309	06/08/1995	PCT	C07D	207/16	Y
	ВН	JP 4334357	11/20/1992	Japan	C07C	233/57	Abstract only
1.	BI	WO 93/08259	04/29/1993	PCT	C12N		Y
	ВЈ	WO 95/11689	05/04/1995	PCT	A61K	37/00	Y
	BK	WO 97/45117	12/04/1997	PCT	A61K	31/435	Y
	BL	DE 196 16 486 C2	10/30/1997	Germany	A61K	45/00	Y
	ВМ	WO 95/29691	11/09/1995	PCT	A61K	38/00	Y
	BN	WO 98/22494	05/28/1998	PCT	C07K	5/06	Y
	во	WO 00/01849	01/13/2000	PCT	C12Q	1/68	Y
	BP	EP 0 658 568 A1	06/21/1995	EPO	C07K	14/605	Y
	BQ	DD 296 075 A5	11/21/1991	Germany	C07D	295/04	Y
	BR	DD 296 075 A5	11/21/1991	Germany	C07D	295/04	N
Ih	BS	EP 0 708 179 A2	04/24/1996	EPO	CI2N	15/16	Y
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			FOREIGN P	ATENT DOCUMENTS			
W		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRAN Y/N
	ВТ	EP 0 995 440 A1	04/26/2000	EPO	A61K	. 31/425	N
	BU	WO 91/11457	08/08/1991	PCT	C07K	7/34	Y
1	BV	WO 91/16339	10/31/1991	PCT	C07K	5/10	Y
	BW	WO 98/19998	05/14/1998	PCT	C07D	207/00	Y
	BX	WO 91/17767	11/28/1991	PCT	A61K	37/54	Y
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	BAA	DE 299 09 210 U	09/09/1999	Germany	A61K	31/425	N
	BAB	DE 198 26 972 A1	12/23/1999	Germany	A61K	38/05	N
	BAC	WO 01/97808	12/27/2001	PCT	A61K	31/425	Y
	BAD	WO 01/34594 A1	05/17/2001	PCT	C07D	401/06	Y
	BAE	WO 00/10549	03/02/2000	PCT	A61K	31/00	Y
	BAF	WO 01/74299 A2	10/11/2001	PCT	A61K	·	Y
	BAG	WO 02/20825 A1	03/14/2002	PCT	C12Q	1/00	Y
	ВАН	WO 01/89569 A1	11/29/2001	PCT	A61K	45/06	Y
	BAI	WO 99/62914	12/09/1999	PCT	C07F	5/02	Y
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	BAK	EP 1 130 022 A1	09/15/2001	EPO	C07D	498/09	Y
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	BAN	WO 01/94310 A1	12/13/2001	PCT	C07D	209/12	Y
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•			FILING DATE: October 1, 2003	ART UNIT: Not Yet Assigned	
		OTHER DOCUMENTS (INCLUDING A	UTHOR, TITLE, DATE, PERTINEN	T PAGES, ETC.)	
IG/ I	CA	Campbell, I.W. New Antidiabetic Drugs, edefficacy and inadequacy". 3:33-51 (1990).	l. C.J. Bailey & P.R. Flatt, Smith-Gordon	a, "Sulphonylureas and metformin:	
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	CC	CHEMICAL ABSTRACTS, vol. 118, no. 2: Hosoda, et al, "Preparation of N-(heterocycl November 1992 (1992-11-20)	5, 21. June 1993 (1993-06-21) Columbus ic Carbonyl) Amino Acids and Analogs	s, Ohio, US; abstract no. 255342k, as Prolyl Endopeptidase Inhibitors",	
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	CF	AMASHEH, S., et al., "Electrophysiologica expressed in Xenopus Laevis oocytes". J. P	l analysis of the function of the mammal <u>hysiol</u> . 504, 169-174 (1997)	ian renal peptide transporter	
	CG	Arai ET AL., "Synthesis of prolyl endopeptivitro inhibition of prolyl endopeptidase from 41, No. 9, 1993, pages. 1583-1588.	idase inhibitors and evaluation of their st n Canine Brain" <u>CHEMICAL AND PHA</u>	ructure-activity relationships: in RMACEUTICAL BULLETIN., Bd.	
	СН	DURINX, C.; et al.; "Reference Values for Laboratory Parameters". Clin Chem Lab M	Plasma Dipepidyl-Pepidase IV activity a led 2001, February; 39 (2):155-9, 1 page	nd their Association with Other	
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	CJ				
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	CL	Lin, J. et al.: "Inhibition of depeptidyl peptidase IV by fluoroolefin-containing n-peptidyl-O-hydroxylamine peptidomimetics" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, Vol. 95, November 1998, pages 14020-14024.			
	СМ	CM KOROM, S., et al "Inhibition of CD26/dipeptidyl peptidase IV activity in vivo prolongs cardiac allograft survival in rat recipients", <u>Transplantation</u> , Vol. 63, 1495 7 1500 No. 10 (1997)			
	CN	MAGYAR, C.E. et al., "Proximal Tubule Na Transporter Responses are the same during Acute and Chronic Hypertension." Am J. Physiol Renal Physiol, 2000, August; 279 (2):F358-69, 1 page.			
ile	со	Martindale The Extra Pharmacopoeia, 30th I	Edition, London Pharmaceutical Press, 19	993, Page 36.	
Examin	er:	W- Weelt	Date: 7 2U	-05 ⁻	

						
. IN	FORIVIA	FORM PTO-1449 TION DISCLOSURE STATEMENT		OCKET NO. -DIV-CON	SERIAL NO. 10/676,832	
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•			_	G DATE: er 1, 2003	ART UNIT: Not Yet Assigned	
		OTHER DOCUMENTS (INCLUDING A	UTHOR, TITLE,	DATE, PERTINENT	PAGES, ETC.)	
(a)	CP	MENTLEIN, R., et al., "Proteolytic processi Pept. 49, 133 -144 (1993)	ng of neuropeptide	Y and peptide YY by	dipeptidyl peptidase IV". Regul.	
	CQ	PAPIES, B. et al., "Isoenzyme (Lactate Dehy Activity Changes in Blood Plasma Likely Inc 1991; 33 (3):218-26, 1 page.	ydrogenase, Asparta dicative of Organ In	nte Aminotransferase) nvolvement due to Art	and Dipeptidyl Peptidase IV erial Hypertension." Cor Vasa,	
	CR	QURESHI. N.U.; et al., "Endogenous Neuro Shock". Regul Pept, 1998, September 25; 7	peptide Y Mediates 5-76:215-20, 1 pag	Vasoconstriction dur	ing Endotoxic and Hemorrhagic	
,	CS	TANKA, S., et al., "Suppression of arthritis" 19, No. 1 Pages 15-24, (1997)	by the inhibitors of	dipeptidyl peptidase I	V". <u>Int. J. Immunopharmacol,</u> Vol.	
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	CU	The Merck Index, 12th Edition, An Encyclop	edia of Chemicals,	Drugs, and Biological	s, 1996, Page 1014.	
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	CAD	Mannucci et al., <u>Diabetes Care</u> , "Effect of Metformin on Glucagon-Like Peptide 1 (GLP-1) and Leptin Levels in Obese Nondiabetic Subjects", 24(3): 489-494, March 2001.				
	CAE	Nauck et al., <u>Diabetologia</u> , "Normalization of in Type 2 (non-insulin-dependent) diabetic p	of fasting hyperglycoatients", (1993), 30	aemia by exogenous g 5: 741-744.	glucagon-like peptide 1 (7-36 amide)	
Nex	CAF	Pauly et al., Regulatory Peptides, "Abstracts Peptides", July 15, 1996, 64(1-3): 148 plus of	s Issue: Abstracts fr	om the 11 th Internation	nal Symposium on Regulatory	
Examin	er:	w. We Ale		Date: 1-64-0	<u> </u>	

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			APPLICANT(S): Demuth et al.			
•			FILING DATE: October 1, 2003	ART UNIT: Not Yet Assigned		
	•	OTHER DOCUMENTS (INCLUDING AU	THOR, TITLE, DATE, PERTINEN	NT PAGES, ETC.)		
(0)	CAG	Stryer, Biochemistry 3 rd Ed., "Protein Conform	mation, Dynamics, and Function", 198	8, p 191-193.		
	САН	T.J. Kieffer et al., "Degradation of Glucose-D In Vitro and In Vivo by DP IV", Endocrinolo	ependent Insulinotropic Polypetide an gy, Vol. 136(8), (1995), p 3585-3596.	d Truncated Glucagon-Like Peptide 1		
	CAI	The Merck Index, An Encyclopedia of Chemi	cals and Drugs, 9th Edition, Merck & O	Co., Inc., 1976, page 773		
	CAJ	C.B. Welch, Medical Management of Non-Instance Association, "Diagnosis and Classification" p	sulin-Dependent (Type II) Diabetes, 3° p. 3, 1994, Pharmacologic Intervention	dedition, American Diabetes (2 pages).		
	CAK	WETZEL, W., et al., "Effects of the CLIP fra Neuropeptides, 31, 41- 45 (1997)	gment ACTH 20-24 on the duration of	REM sleep episodes".		
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			APPLICANT(S): Demuth et	al.		
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